XXXY Chromosomal Abnormality in a Child

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IT IS ESTIMATED that a chromosomal abnormality occurs in approximately one of every one to two hundred live births.[4,5,6] About three-fourths of these abnormalities involve the sex chromosomes. The affected children may present problems of physical development and mental retardation. Early recognition and diagnosis offers the opportunity to give genetic counselling regarding future pregnancies and to plan for special training which will permit these children to reach their full potential. The following is a case report of a boy three years and nine months of age with XXXY sex chromosomal abnormality. This is believed to be the youngest age at which this anomaly has been reported.

Report of a Case

The propositus is a three year, nine month old male of Dutch-Indonesian parentage. He was born at nine months of gestation to a para 0, gravida 1 mother 25 years of age. The prenatal period was not complicated by bleeding, infection, x-ray exposure, drugs, or systemic disease. The delivery was normal and the baby, who weighed 6 pounds 5 ounces, cried spontaneously. No significant physical findings were noted at the time of birth except for a bilateral forefoot adduction. External genitalia were considered normal.

The development of the child included the following milestones: head-holding a 5¾ months, turning over at 6¾ months, crawling at eight months but with poor use of legs, sitting without support at 10 months, first tooth eruption at one year, walking alone at two years with a waddling gait and tendency to walk on tiptoes and frequent falling, and bowel and toilet training at 3½ years. Speech development included first words at 18 months (mama), and two to three word sentences and naming a few colors at 3½ years. The growth pattern revealed the child to be consistently small in weight and stature. At one year he weighed 16 pounds (below the third percentile) and was 29¾ inches tall (fiftieth percentile). At 3½ years he weighed 32 pounds (fiftieth percentile) and was 38¾ inches tall (twenty-fifth percentile).

The family history was not remarkable. Siblings include normal identical twin boys one year of age. There was no family history of congenital defects, chromosomal abnormalities, consanguinity, infertility or mental retardation.

The patient's history of childhood illnesses was unremarkable except for left esotropia with decreased abduction of the eye at six months of age, persistent vomiting at 23 months of age (with normal gastrointestinal and thoracic x-ray studies) which subsided spontaneously, orthopedic consultation for the forefoot adduction, and three days in hospital at 3⅓ years for bronchitis.

Physical examination at 3½ years revealed the following pertinent findings: The child was a thin, friendly, responsive and cooperative boy with peculiar facies due to eye-wide medial epicanthal folds and prominent lateral epicanthal folds. No esotropia was present. The mouth and teeth were normal and without a high arched plate. Heart, lungs and thoracic cage revealed no abnormalities. Testicles were palpable bilaterally and were judged to be of normal size. The penis was small and circumsized. The elbow joints were held in a position of cubital varus, with limited supination, and crepitus could be felt on pronation (Figure 1). The hands revealed no simian crease but showed incurving of the fifth fingers bilaterally. The hips were hyperextensible. The feet had a mild bilateral varus. Neurological examination was negative except for symmetrically hypoactive deep tendon reflexes. Cranial nerves were normal. Psychological testing revealed an I.Q. of 60.

Recent laboratory findings included normal blood cell count and protein-bound iodine of 5.5 mcg per 100 ml. X-ray films of the elbow joints showed radial-ulnar synostosis (Figure 2). A chromosomal preparation of peripheral blood leu-

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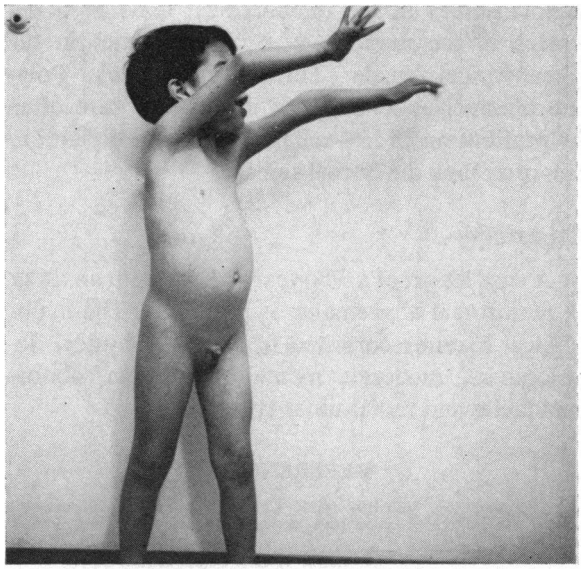

Figure 1.—Child at age of 3¾ years with elbow joints held in position of cubital varus.

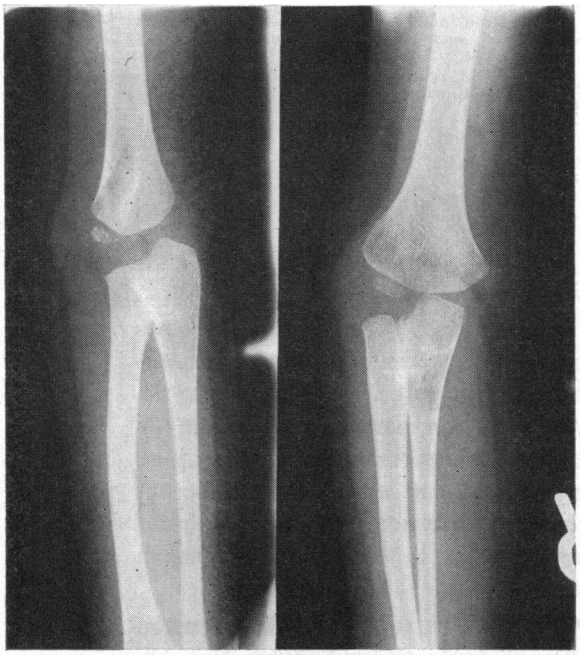

Figure 2.—X-ray film of elbows showing radial-ulnar synostosis.

kocytes revealed an XXXY sex chromosomal abnormality. The autosomal chromosomes were normal in distribution and morphologically (Figure 3). Buccal smears revealed two Barr bodies in most cells. On study of polymorphonuclear leukocytes, female "drumsticks" were noted in 9 percent of the cells.

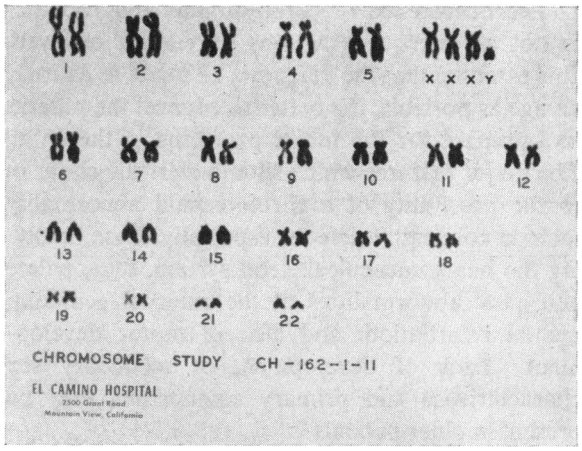

Figure 3.—Chromosomal karyotype with an XXXY chromosomal abnormality and normal autosomal chromosomes.

Discussion

The XXXY sex chromosomal abnormality is generally regarded as a variant of Klinefelter's syndrome (XXY). As a general rule, the degree of physical abnormalities and mental retardation increases as the number of X-chromosomes increases. The patient in the present case follows this pattern. The physical findings in the XXXY cases are more pronounced than the infantile sexual development and borderline low mentality of the Klinefelter's syndrome but not as great as the gross physical abnormalities and severe mental retardation of the XXXXY chromosomal abnormality. The age of diagnosis is also directly related to the severity of the abnormalities. Most cases of true Klinefelter's syndrome are not diagnosed until puberty, when the lack of secondary sex characteristics becomes obvious. This is true also of previously reported cases of the XXXY variant, the age at diagnosis having been reported at from 14 to 22 years.[1,2,3] All the patients have had significant degrees of mental retardation. The patient in the present case is the youngest yet reported with the XXXY abnormality.

The origin of the abnormality appears to be a double nondisjunction of the X chromosome occurring in the first and second meiotic divisions. While it is possible that the defect may occur in either the ovum or sperm, most of the evidence supports maternal origin. Since it is the result of a sporadic nondisjunction, it is not hereditary and the parents can be reasonably reassured that future pregnancies are not likely to result in a similarly abnormal child.

The occurrence of chromosomal abnormalities is not as infrequent as was previously believed. It is essential that the diagnosis be made at as early an age as possible, the better to counsel the parents and prepare for the future problems of the child. The major features which should alert the clinician to the possibility of a chromosomal abnormality include congenital defects, especially those involving the heart, musculoskeletal system, face, palate and ears; abnormalities of the external genitalia; mental retardation; and lack of motor development. Lack of development of secondary sex characteristics and primary amenorrhea may be present in older patients.

The diagnosis of specific chromosomal abnormalities can be made with certainty only by chromosomal analysis. Peripheral blood leukocytes are easily obtainable for chromosomal cultures and are entirely satisfactory for most problems. Chromosomal analysis is now readily available at most major medical centers, at many of the larger hospitals and at commercial laboratories. The examination of buccal smears for Barr bodies is a good screening procedure for sex chromosomal abnormalities involving an increase in the number of X chromosomes in the phenotypical male or a decrease in the number of X chromosomes in the phenotypical female (Turner's syndrome). Polymorphonuclear leukocytic "drumsticks" are often helpful but much less reliable and more difficult to interpret than the buccal smears.

Summary

A case report of a 3¾ year old boy with an XXXY chromosomal abnormality is presented. The major clinical features consisted of delayed physical development, moderate mental retardation, abnormal facies and radial-ulnar synostosis.

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THE EMERGENCY OF TAMPONADE

"A cardiac injury requires no treatment in the emergency room if there's no evidence of tamponade or continuing hemorrhage. However, patients are monitored quite closely for venous pressure in the intensive care unit right next to the operating room. If they do show evidence of tamponade, pericardiocentesis is the primary method of management. If the patient does not respond immediately or if tamponade recurs, immediate thoracotomy is performed without letting the patient arrest. If arrest should occur by any method of treatment, at any time, thoracotomy is immediately performed, whether on the ward, in the operating room, in the emergency room, or in the intensive care unit."

—ARTHUR C. BEALL, JR., M.D., Houston

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